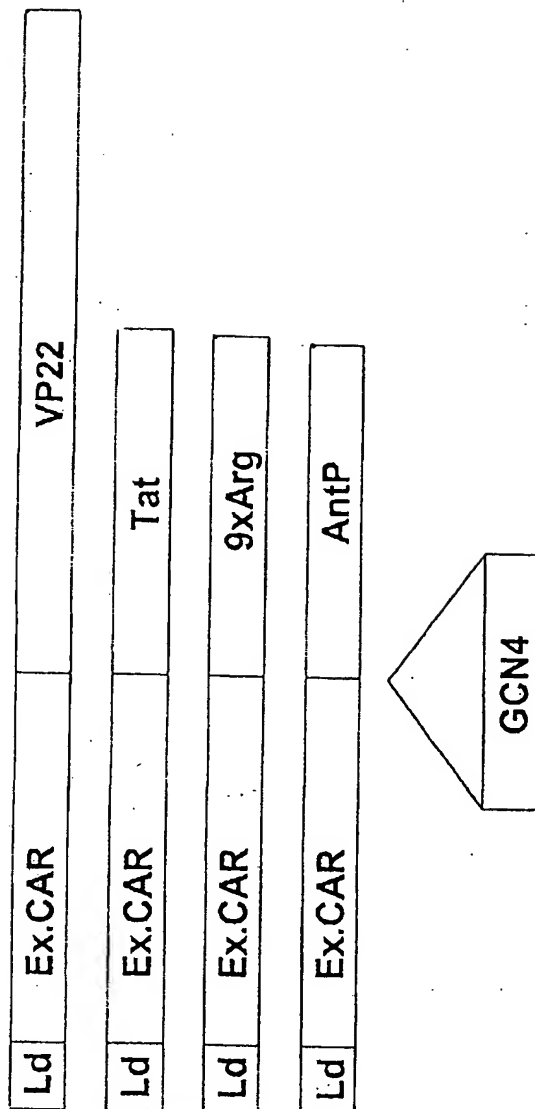




Figure 1

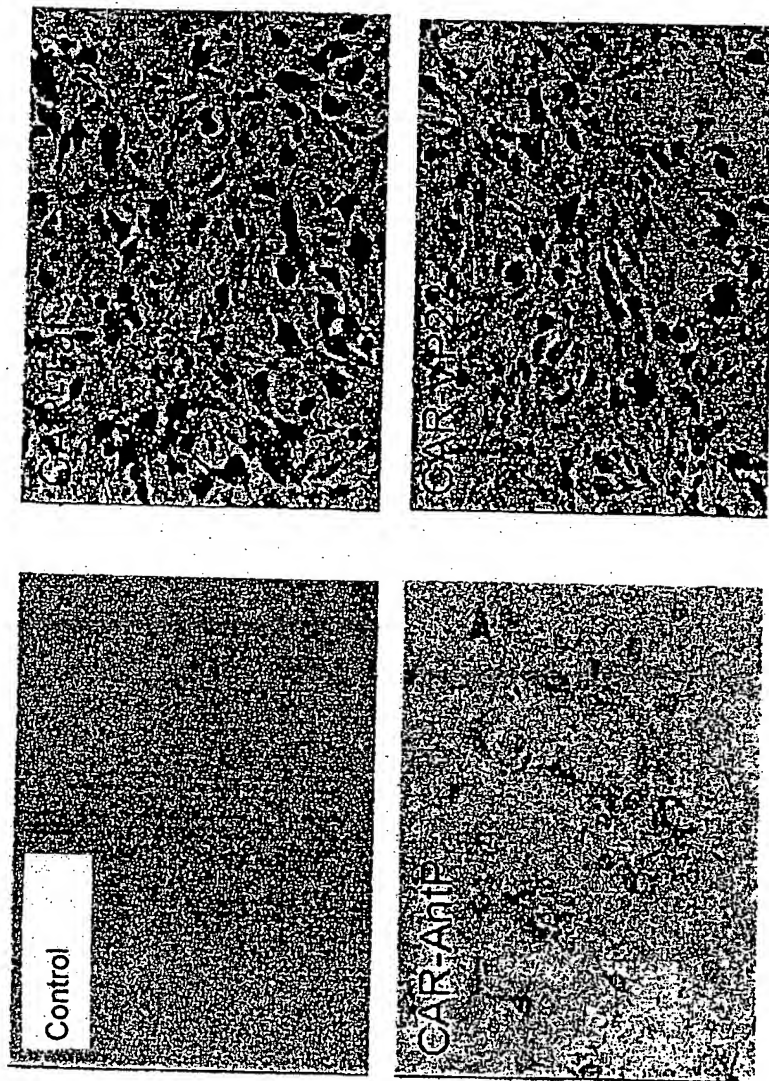
Construction diagram



Legend:

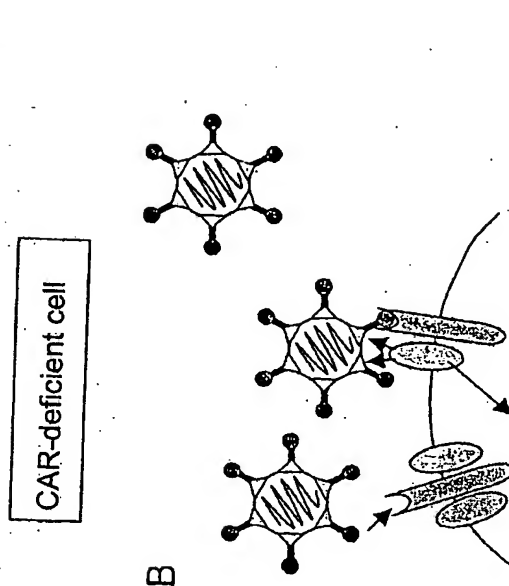
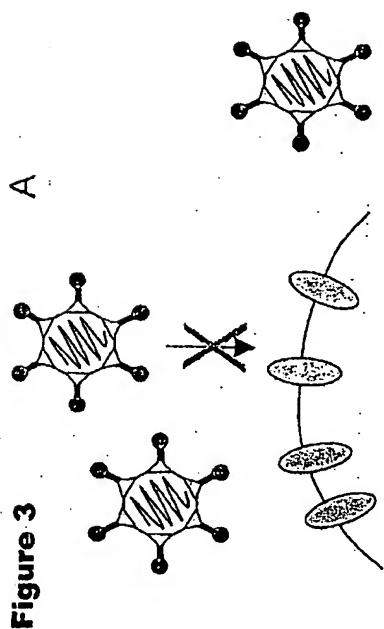
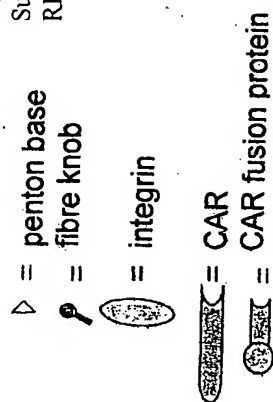
- Ld** = natural leader sequence of the coxsackie adenovirus receptor for synthesis of the protein into the endoplasmic reticulum
- Ex.CAR** = extracellular domain of the coxsackie adenovirus receptor
- GCN4** = optional insertion of an oligomerization domain (here GCN4 as an example) for possible intensification of the CAR/fibre knob affinity

Figure 2



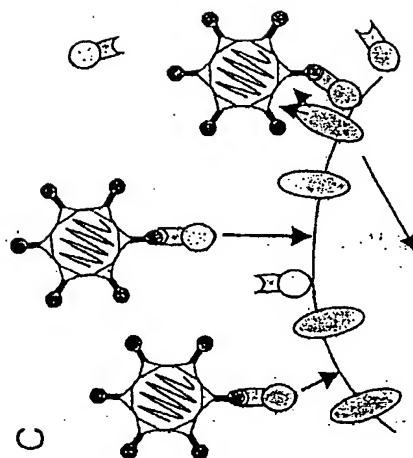
Fusion proteins from the extracellular domain of the Coxsackie adenovirus receptor and basic peptides or VP22 increase the adenoviral infection of CAR-deficient NIH3T3 fibroblasts.

293 cells were transfected with expression constructs for the fusion proteins shown in the figure (pBluescript as a control). After 36 h the supernatants of the cell layer were removed and mixed with LacZ-transgenic adenoviruses (Ad-LacZ). Thereafter, NIH3T3 fibroblasts were infected with this mixture. The multiplicity of infection (MOI) here was 10. After 48 h the infected NIH3T3 cell layer was analysed for β -galactosidase expression by blue staining by X-gal substrate conversion in order to demonstrate the viral infection



CAR binds the hexon protein of the viral particle, penton-bound integrin consequently gives the signal for internalization via endocytosis

CAR-expressing cell



CAR fusion protein bound to the adenoviral hexon protein directs and sticks the particle to the cell membrane. Integrins consequently bind to the adenoviral penton protein as a signal for the internalization of the particle via endocytosis

CAR-deficient cell in the presence of CAR fusion proteins

Figure 4

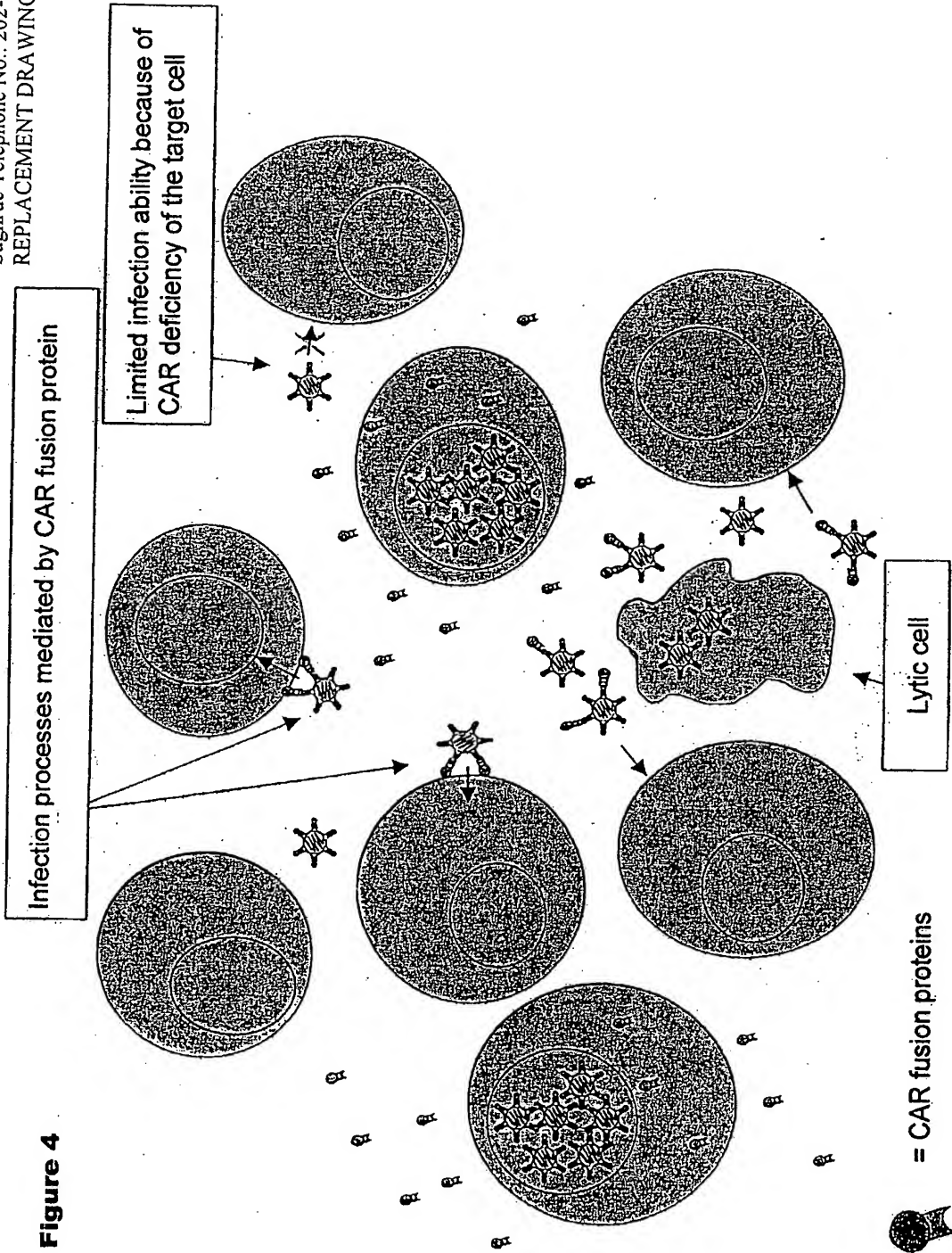
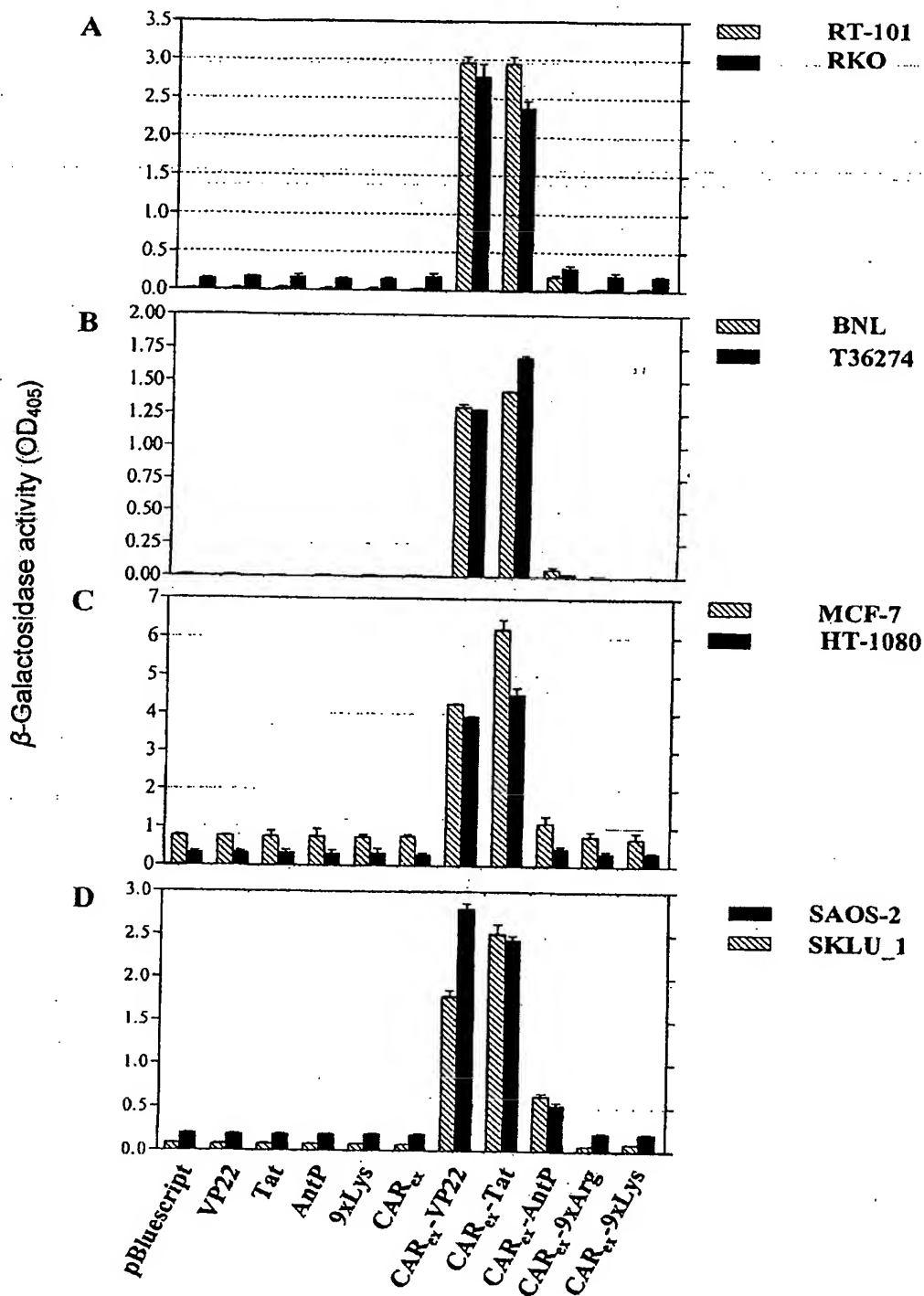


Fig. 5: Infection efficiency of various cell lines



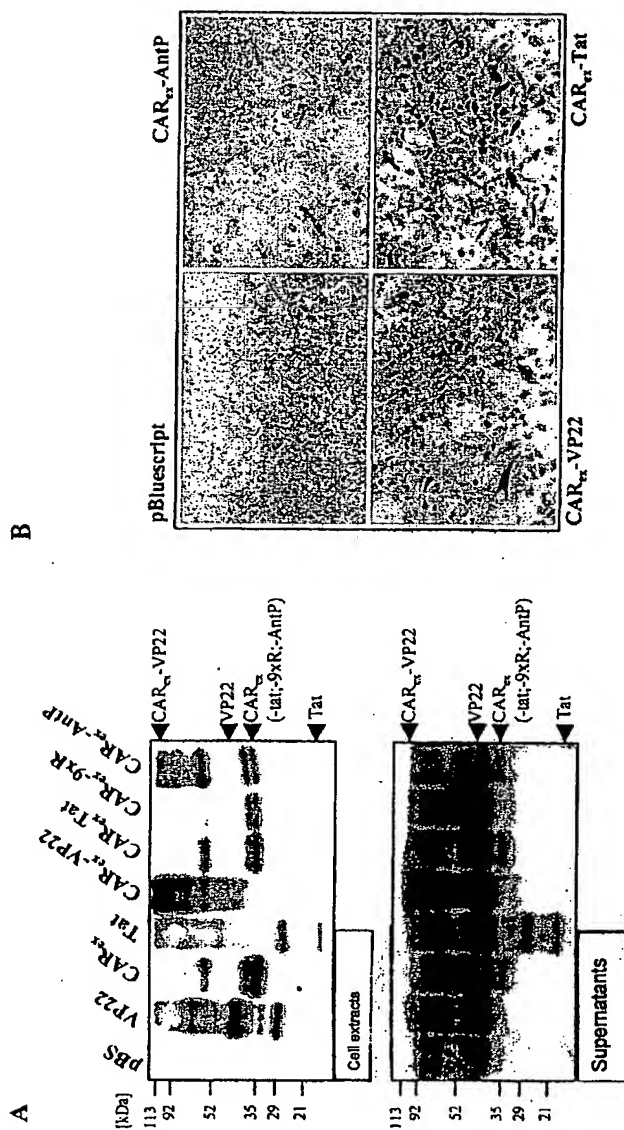


Fig. 6

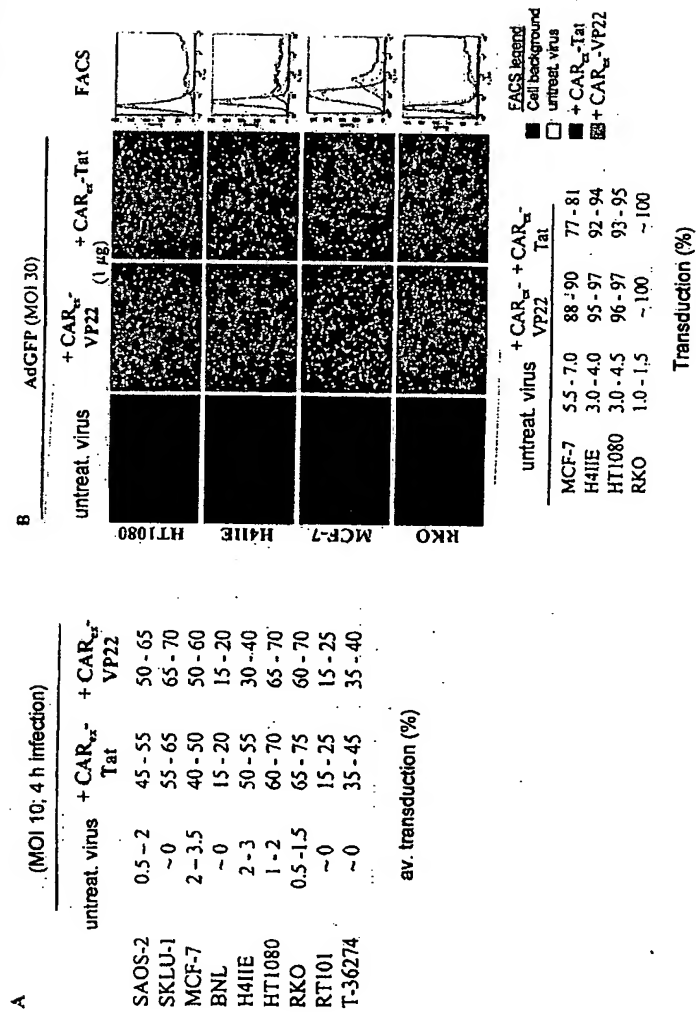


Fig. 7

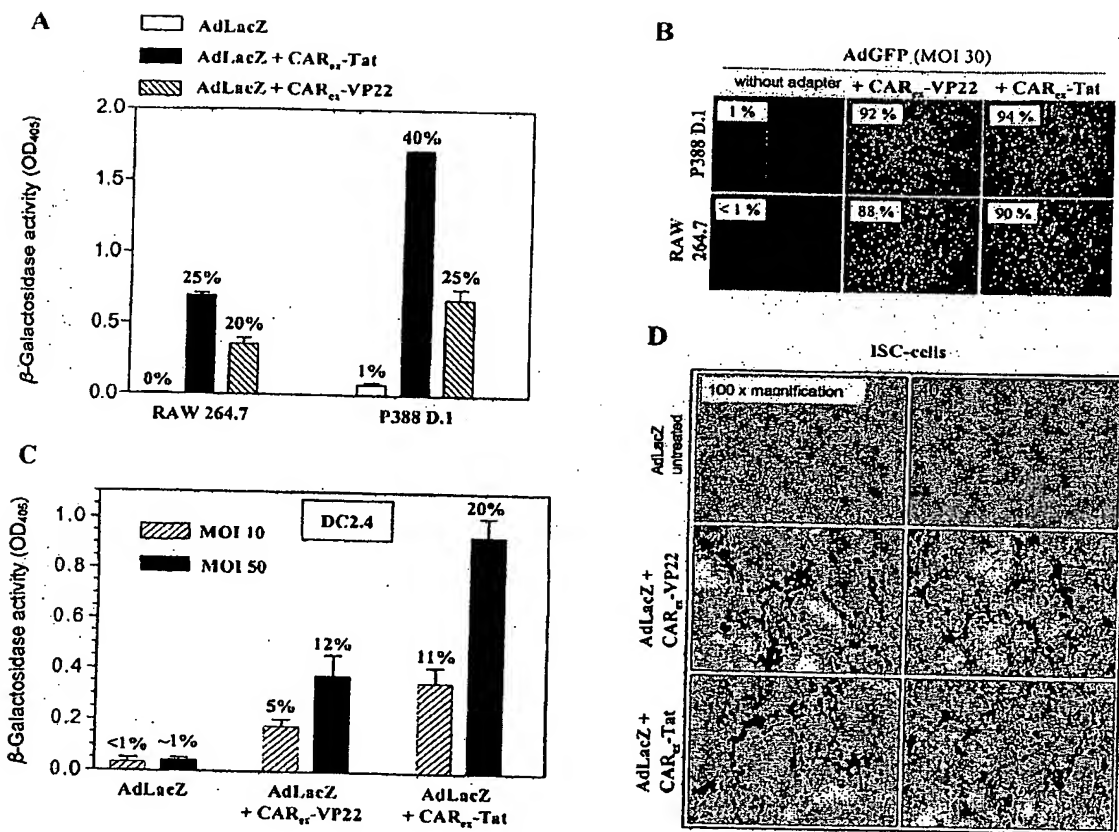


Fig. 8

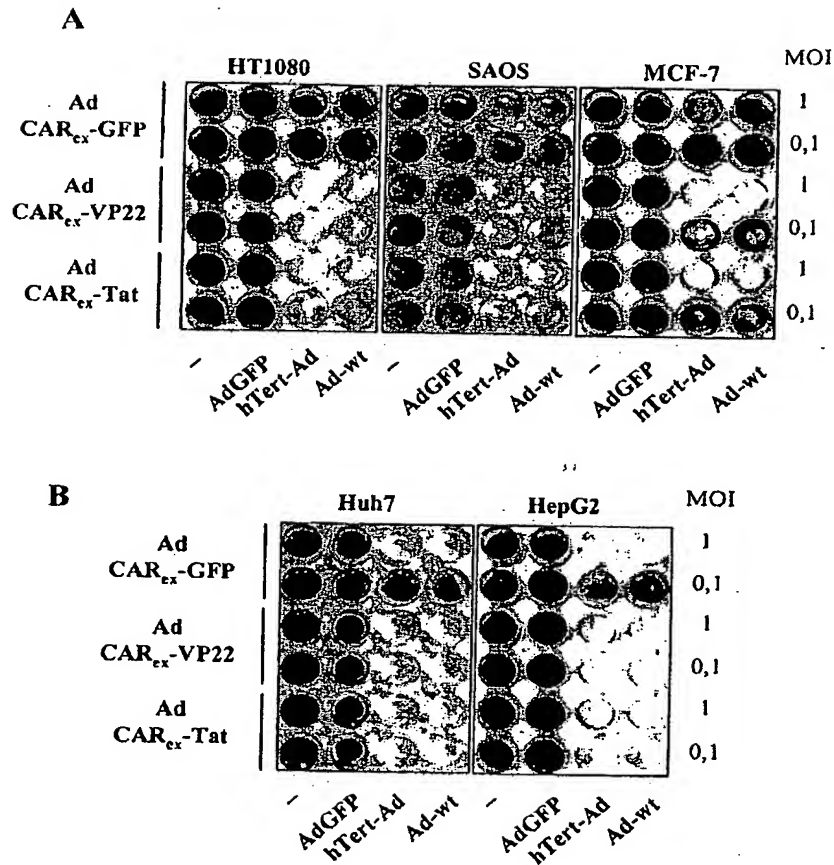


Fig. 9

U.S. Patent Application No. 10/583,249
 Inventor(s): Stephan KUBICKA
 Filed: June 16, 2006 Art Unit: Not yet assigned
 For: MEDIZINISCHE HOCHSCHULE HANNOVER
 Attorney Docket: Q95566
 Sughrue Telephone No.: 202-293-7060
 REPLACEMENT DRAWING Fig. 10

AdGFP

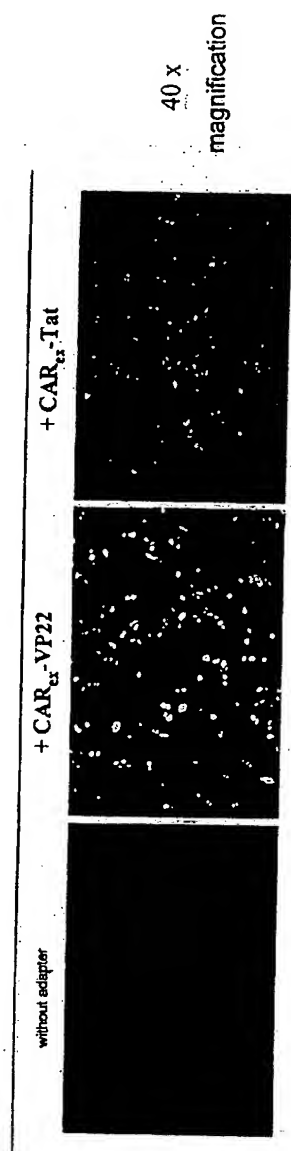


Fig. 10

Fig. 11: Influence of the pH

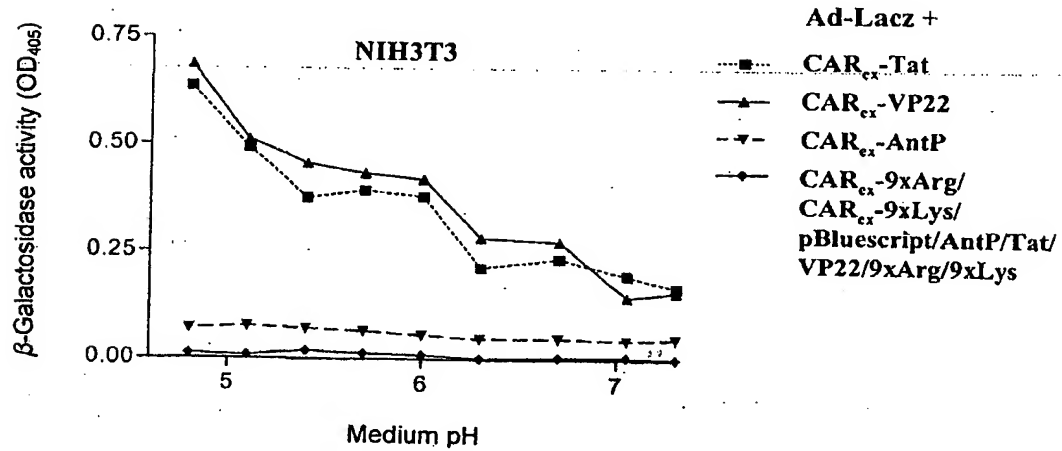


Fig. 12: Influence of the time delay

